REMARKS

Reconsideration and withdrawal of the pending rejection under 35 U.S.C. §103(a) are respectfully requested.

Rejection under 35 U.S.C. §103(a)

At page 2, the Office Action maintained a rejection under 35 U.S.C. §103(a). Applicants present evidence below demonstrating that the rejection and more specifically the maintenance of the rejection were in error.

The instant rejection relies on the passage from the St. George-Hyslop applied reference that was quoted at page 3 of the Office Action and reproduced below.

> The normal PS1 protein, substantially free of other proteins, is encoded by the aforementioned SEQ. ID No:1 and SEQ ID NO:133. As will be later discussed, PS1 protein and fragments thereof may be made by a variety of methods. Purified **mutant** PS1 protein is characterized by FAD--associated phenotype (necrotic death, **apoptotic** death, granulovascular degeneration, neurofibrillary degeneration, abnormalities or changes in the metabolism of APP, Ca.sup.2+, K.sup.+, and glucose, mitochondrial function and energy metabolism neurotransmitter metabolism, all of which have been found to be abnormal in human brain, and/or **peripheral tissue cells** in subjects with Alzheimer's Disease) in a variety of cells. The mutant PS 1, free of other proteins, is encoded by the mutant DNA sequence. [Emphases in Office Action]

At page 5, lines 12-16, the Office Action explains the basis for rejection as follows:

> With regard to Applicant indicating that there is no reasonable expectation of success that the cells designed for production would apoptose (Applicant's response, page 5), this is not persuasive because St. George-Hyslop et al. teaches that cells that overexpress mutant presenilin apoptose (see St. George-Hyslop et ai., col. 20, 3rd parag.).

Applicants respectfully refer to the St. George-Hyslop passage which states "(necrotic death, apoptotic death, . . . all of which have been found to be abnormal in human brain, and/or peripheral tissue cells in subjects with Alzheimer's Disease)". The plain language of the quoted

reference indeed indicates that a menu list of events has been observed in "brain, and/or peripheral tissue cells" but does not indicate where, for example, necrotic death, occurs and under what conditions and where apoptotic death occurs and under what conditions. Thus relying on the plain language of the applied reference as evidence it cannot properly be concluded that "St. George-Hyslop et al. teaches that cells that overexpress mutant presenilin apoptose". The reference does not distinguish at least between necrotic death and apoptotic death and also does not clearly indicate which of the menu of events occur in which tissues. When properly read, the St. George-Hyslop passage cannot properly be relied upon as applied to support the instant rejection. In view of this clarification, reconsideration and withdrawal of this rejection are respectfully requested.

Conclusion

In view of the above remarks, Applicants respectfully submit that the application is now in condition for allowance and request prompt issuance of a Notice of Allowance. Should the Examiner wish to suggest additional changes that might put the application in even better condition for allowance, the Examiner is requested to contact the undersigned at the telephone number listed below.

Fees

The Commissioner is hereby authorized to charge any fee required for added claims and any additional fees that may be needed to Deposit Account No. 18-1982.

Respectfully submitted,

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